RESEARCH PRIORITIES

Farm Animal Research in Crisis

Inadequate funding threatens vital agricultural and biomedical research with farm animals.

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The annual economic value of livestock and poultry sales in the United States currently exceeds $132 billion (*1*), yet only about 0.04% ($32.15 million) (*2*) of the $88 billion Department of Agriculture (USDA) budget in fiscal year 2007 (*3*) was allocated to its competitive grants program for research that directly involves agriculturally important domestic animals. By contrast, the Department of Health and Human Services (DHHS) apportioned 4.1% ($29.5 billion) of its $716 billion budget in fiscal year 2008 to the National Institutes of Health (NIH) of which ~80% supported extramural research (*4*). Whether this direct comparison between USDA and DHHS is appropriate may be debatable; still, it clearly illustrates the huge disparity in total budget available for research grants focused on animal agriculture, about 1/918th that for human health. The private sector does invest in agricultural research and development, but, understandably, such funds are highly focused on commercial interests and not on basic research of the kind we discuss.

The Hatch Act of 1887 provided the USDA with the first mandate to sponsor extramural research in the United States. It funds federal laboratories and provides annual support to state agricultural colleges through a formula based on each state's share of rural and farm populations. In general, "formula funds" support little fundamental research, but instead are focused on applied, mission-orientated programs, teaching, and extension of information to the public in the nation's land-grant colleges. Although this formula for distributing funds may be outmoded, the program has been largely responsible for the strength of U.S. agricultural research.

As time has passed, however, Hatch funds and other research formula funds, even with the help of matching dollars from states, have declined markedly in constant dollars and have been insufficient to maintain research farms and other infrastructure—let alone the research programs—necessary for colleges of agriculture to remain viable (*5*). Instead, faculty researchers have been obliged to seek alternative sources of funds to support their programs, including "earmarks" from influential lawmakers.

FARM ANIMALS AS BIOMEDICAL MODELS

Obesity	Ovarian cancer
Diabetes	Nutrition
Aging	Immunology
Cardiovascular disorders	Genomics
Infectious disease	Therapeutics
Neurobiology	Ophthamology
Epigenetics & environment	Reproduction

Research areas that could potentially be advanced by using farm animals as biomedical models. For appropriate farm animal models for specific diseases and references, see www.adsbm.msu.edu.

Unfortunately, the U.S. Congress failed to authorize USDA to conduct a well-funded, comprehensive, peer-reviewed, competitive grants program for agriculture after World War II. Indeed, in its first report in 1972 (*6*), the National Research Council (NRC) warned ominously that "grossly inadequate support has been given to the basic sciences that underpin agriculture." Subsequent reports echoed this same theme (*7*, *8*). Nonetheless, the forerunner of the present-day competitive USDA grants program grew out of the NRC report and has funded many notable advances in agricultural practices for increased food safety, reproductive efficiencies, and diets to meet specific animal production systems. Since 1990, this program has been called the National Research Initiative or NRI, and it currently supports studies in domestic species, from applied to very basic mechanistic and molecular studies. In October 2009, a new granting body, The National Institute for Food and Agriculture will be established to replace the USDA CSREES (Cooperative State, Research, and Education Service).

Furthermore, as of 1 October 2008, the NRI was replaced by a new competitive grants program for agriculture, the Agriculture and Food Research Initiative (AFRI), which has a greater level of congressionally authorized funding in the farm bill (e.g., $700 million per year for AFRI versus $500 million per year for the NRI). However, an appropriation exceeding $150 million is only a fairly recent event (*9*), and the total AFRI budget in the 2009 appropriation only amounted to $201.5 million (*10*). Moreover, in contrast to NIH, AFRI received no funding from the recently enacted economic stimulus package. Thus, it remains to be seen whether the change in title and mandate of the agency will improve future prospects for research on farm animals and whether the congressionally authorized $700 million per year in funding for AFRI will be appropriated.

Dismal funding for basic mechanistic and molecular research in farm animals has paralleled other trends within colleges of agriculture and departments of animal sciences. In the last two decades, there has been a 44% decrease in research support from federal and state agencies (*5*). Faculty positions in animal science departments at some of the larger land-grant institutions have fallen by more than 50% over the last 30 years. That this decline is systemic is supported by NSF's Survey of Earned Doctorates, which indicates that awarded doctorate degrees in the animal sciences declined 30% from 1985

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to 2004 (*11, 12*). In addition, enrollment in Master's and Ph.D. programs declined 9 and 16%, respectively, between 2004 and 2006 alone (*12*). Equally troubling is the rapid disappearance of breeds and genetic lines of domestic species, especially evident for poultry (*13*); these are irreplaceable genetic resources.

Are farm animals really necessary to advance biomedical research? Seventeen Nobel Prize winners have used farm animals such as cattle, pigs, sheep, goats, horses, and chickens as research models (*14*), yet their value is generally underappreciated. Recently, application of the tools of genetic manipulation and extending genome sequencing efforts in farm animal species [e.g., the published sequence for the bovine (*15*) and for the chicken (*16*) genomes and ongoing sequencing efforts in swine (http://piggenome.org/index.php)] have provided new opportunities. The data will generate insights not only into gene function, but also into genetic and environmental influences on animal production and human disease.

There are numerous examples of compelling domestic species models relevant to diverse areas of biomedical research, including comparative physiology and genomics, cloning, artificial insemination, "biopharming" to produce high-value pharmaceuticals in milk, osteoporosis, diabetes-induced accelerated atherosclerosis, asthma, sepsis, alcoholism, and melanoma (see figure). Because of their size and relatively long generation interval, domestic species such as sheep are widely used to unravel the mechanisms whereby the environment (e.g., diet, temperature, and toxicants) may "program" the developing embryo and fetus, resulting in adult onset of disease (*17*, *18*). Mice with a disrupted *CFTR* gene are helpful in studying some aspects of cystic fibrosis, but they fail to develop the hallmark pancreatic, lung, and intestinal obstructions that occur in humans. The *CFTR* knockout pig model, derived by somatic cell nuclear transfer using *CFTR*-null fibroblasts, better mimics human pathology than do mouse models (*19*). The baby pig is the model of choice for research on human infant nutrition, and swine also develop chronic diseases (atherosclerosis, gastric ulcers, and obesity) observed in humans (*20*). Further, size does matter when it comes to animal models. Surgery, blood sampling, tissue recovery, serial biopsies, instrumentation, whole-organ manipulations, cloning, and many other biomedical applications (*21*) are more easily achieved in animals larger than a mouse.

As pointed out in recent commentaries (*5*, *22*), the number of scientists trained to work with large animal models is decreasing along with numbers of research centers. There is also an idiosyncratic, but long-standing, "cultural" segregation between colleges of agriculture and colleges of human medicine, veterinary medicine, and the basic life sciences disciplines, even when all are located on the same campus. This situation has diminished collaboration and often has failed to challenge traditional animal science thinking. At many institutions, the isolation of animal science programs has, we believe, contributed to poor recruitment of top-notch researchers with an appreciation of newer and emerging technologies.

There also are perceived concerns, raised during recent USDA- and NIH-sponsored workshops (www.adsbm.msu.edu), that proposed uses of agricultural species as models for biomedical research are not received well by NIH study sections and require more extensive justification than research proposed using rodent models. An analysis of funded NIH grants from 2002 to 2006 that made use of animals revealed that ~98% employed rodents, primarily mice, whereas the already small number of funded grants that used farm animals declined by 30% (*5*). The mouse is now overwhelmingly the comparative animal model of choice in such studies because its small size and relatively low cost of maintenance trump the numerous attributes of the cows, sheep, pigs, and other farm animals as valuable biomedical models. But, the economic value of farm animals often offsets much of the associated expenses for their use in research. The mouse, however, reproduces rapidly, has a fully sequenced genome that can be readily manipulated by either adding or knocking out selected genes, and is available as a myriad of inbred and mutant strains. Despite the attractiveness of the mouse, a range of animal models is required to understand how genomes have evolved to drive processes such as reproduction and memory and to extrapolate this genetic information to humans (*23*).

Although a cost-benefit analysis of research specifically on animal agriculture has never been performed, annual returns on federal investment for all agricultural research is reported to be 49 to 62% (*24*). There certainly must also be improved use of existing public funds for the public good. For example, federal agencies should develop joint strategies and adjust portfolios to encourage funding focused on large animal models when appropriate, including establishment of research centers comparable to the NIH-funded National Swine Research Center on the University of Missouri campus. The NIH could develop a funded program committed to advancement of promising alternative animal models, including farm animals. The NIH Center for Scientific Review should ensure that applications that plan to use domestic animal models receive informed input by including individuals with the necessary expertise on review panel rosters. Within colleges of agriculture and veterinary medicine, there should be incentives to recruit nontraditional faculty who are prepared to interact with the broader life sciences community and to pursue funding aggressively from NIH. In particular, administrators must not back away from defending the use of farm animals for both agricultural and biomedical research. The "protected island fortress" of agriculture, usually located on the "other side of campus," is an anachronism that is no longer viable as state and federal support for research with large animal models declines.

References and Notes

1. The 2007 Census of Agriculture, "Economics," www.agcensus.usda.gov/Publications/2007/Online_Highlights/Fact_Sheets/economics.pdf.
2. NRI Competitive Grants Program, www.csrees.usda.gov/funding/nri/pdfs/2007_ann_report.pdf.
3. *USDA FY2007 Budget Summary and Annual Performance Plan*, www.obpa.usda.gov/budsum/fy08budsum.pdf
4. U.S. DHHS, *Budget in Brief*, www.hhs.gov/budget/09budget/2009BudgetInBrief.pdf.
5. J. J. Ireland *et al.*, *J. Anim. Sci.* **86**, 2797 (2008).
6. NRC, *Report of the Committee on Research Advisory to the U.S. Department of Agriculture* (National Academy Press, Washington, DC, 1972).
7. NRC, *Investing in Research: A Proposal to Strengthen the Agricultural, Food and Environment System* (National Academy Press, Washington, DC, 1989).
8. NRC, *National Research Initiative: A Vital Competitive Grants Program in Food, Fiber, and Natural-Resources Research* (National Academies Press, Washington, DC, 2000).
9. M. A. Mirando *et al.*, *Biol. Reprod.* **74**, 459 (2006).
10. *Appropriations Request, National Institute of Food and Agriculture, AFRI;* www.nasulgc-bac.com/documents/FY2010/KB/AFRI.pdf.
11. USDA Research, Education, and Economics Information System, Reports (2007); www.reeis.usda.gov/portal/page?_pageid=193,1&_dad=portal&_schema=PORTAL).
12. Food and Agricultural Education Information System, "Animal Science Graduate Enrollment" (2007); http://faeis.ahnrit.vt.edu/newsletter/december_07/newsletter.html.
13. J. E. Fulton, M. E. Delany, *Science* **300**, 1667 (2003).
14. Foundation for Biomedical Research, *Nobel Prizes*; www.fbresearch.org/Education/NobelPrizes/tabid/427/Default.aspx.
15. The Bovine Genome Sequencing and Analysis Consortium, *Science* **324**, 522 (2009).
16. International Chicken Genome Sequencing Consortium, *Nature* **432**, 695 (2004).
17. A. J. King *et al.*, *Am. J. Physiol. Endocrinol. Metab.* **292**, E1837 (2007).
18. V. Padmanabhan, *Rev. Endocrin. Metab. Disord.* **8**, 67 (2007).
19. C. S. Rogers *et al.*, *Science* **321**, 1837 (2008).
20. D. L. Brooks, P. C. Tillman, S. M. Niemi, in *Laboratory Animal Medicine*, J. G. Fox, B. J. Cohen, F. M. Lowe, Eds. (Academic Press, New York, 2006), pp. 273–295.
21. L. P. Reynolds *et al.*, *J. Nutr.* **139**, 427 (2009).
22. L. P. Reynolds *et al.*, *J. Anim. Sci.* **86**, 2445 (2008).
23. R. Gibbs *et al.*, *Bovine Genomic Sequencing Initiative: Cattle-izing the Human Genome* (NHGRI), NIH, Bethesda, MD, 2004); www.genome.gov/ 12512284.
24. W. E. Huffman, R. E. Evenson, *Am. J. Agr. Econ.* **88**, 783 (2006).

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